Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.53555/88t15k28

ANALYSIS OF DRUG-DRUG INTERACTIONS IN PRESCRIPTIONS FROM A TERTIARY CARE TEACHING HOSPITAL OF NORTH INDIA: AN OBSERVATIONAL STUDY

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Abstract

INTRODUCTION: Managing a disease state often requires multiple medicines simultaneously leading to drug-drug interactions. It results in failure of therapy or toxicity.

OBJECTIVE: To assess prevalence of drug-drug interactions and their desirability to analyse preventable events.

MATERIAL AND METHODS: The study design was a prospective, and observational study. The study included 150 randomly collected prescriptions from the medical outpatient department of a tertiary care teaching hospital in North India, irrespective of gender or diagnosis. The study was conducted in Dec 2023 over a period of 2 months after taking ethical clearance from the Institutional Ethics Committee. Data was collected, tabulated, analysed using descriptive statistics by using Microsoft excel.

Main outcome measured was occurrence of drug-drug interactions.

RESULTS:

Total number of medicines prescribed was 86 types of medicines in 150 prescriptions.

Average medicines prescribed per prescription was 5.6 drugs

Monotherapy was prescribed in 3.3% prescriptions. There were 46.6% prescriptions with less than 5 drugs and 50.1% prescriptions with more than 5 drugs.

The prevalence of drug-drug interactions was 33%(49/150). 30 drug-drug interactions were found related to CVS,13 from Endocrinology, 3 from Antibiotics, 2 from Analgesics, and 1 each from Steroids and CNS drugs respectively.

CONCLUSION: Drug-drug interactions (DDIs) were common and often undesirable, therefore preventable. This study underscores the importance of reducing drug drug interactions in

prescriptions to enhance the quality of healthcare in hospitals. It highlights areas for improvement in prescription practice.

INTRODUCTION:

A Drug interaction refers to the possibility of alteration in the intensity of pharmacological effects of a drug by a factor like co-administration of another drug, a herbal preparation, a food item or a diseased condition. The net result may be an enhanced or diminished effect or appearance of a new effect.

DDIs can be pharmacokinetic i.e. one drug affects the absorption distribution, metabolism or excretion of another, altering its concentration in the body. For e.g. At the level of absorption: Ranitidine –Triazolam, Levothyroxin-antacid, Dabigatran- Verapamil. At the level of metabolism- Statin – Macrolide, Ketoconazole- anti HIV drugs, Steroids – St johns warts, Terfenanadine – erythromycin. At the level of distribution: Aspirin, Barbiturates, Phenytoin, Sulphonamide, Valproic acid and Warfarin. At the level of excretion: Acetaminophen- ethanol, Lithium-Ibuprofen.

Or another type of DDI could be Pharmacodynamic interactions i.e. Drugs act on the same or related pathways, either enhancing (synergistic, additive, potentiation) or reducing (antagonist) effects. For e.g. Beta blocker combinations, ATT regimes are synergistic, Nitroglycerine with phosphodiesterase inhibitors is undesirable interaction.[1]

Polypharmacy refers to the simultaneous use of multiple medications by a patient, typically defined as taking >5 drugs at the same time. It's common among geriatric population as usually they have multiple diseases. Careful monitoring and regular review of the medication regime are essential to avoid potential complications associated with polypharmacy.[2]

Undesirable drug-drug interactions can be misinterpreted as a new medical condition, leading to the prescription of additional medications to treat the side effects, rather than addressing the root cause also known as prescription cascade.[3]

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MATERIALS AND METHODS:

STUDY DESIGN:

Prospective, Observational study.

The study was conducted in the Outpatient Department of a tertiary care teaching hospital of North India after taking ethical clearance (No: GMC/IEC/23/RK/133 ; dated 14/12/23) from the Institutional Ethics Committee. Informed consent was obtained from each patient. Their privacy was strictly maintained throughout the study. 150 prescriptions were randomly collected, irrespective of patient characteristics and diagnosis from various outpatient departments of the hospital. The data from the prescriptions was systematically collected and entered into excel sheet and analyzed for drug-drug interactions. The drugs prescribed by the physician was then counted and average number of drugs prescribed per prescription was calculated. [4]

INCLUSION CRITERIA:

1. All patients attending the OPD irrespective of age and gender.
2. Patients who give a written voluntary consent for the study.

EXCLUSION CRITERIA:

1. Patients attending OPD for vaccination.
2. Patients refusing to provide voluntary written consent for the study.

A copy of each prescription included was kept for record. Data was compiled in excel sheet, in the form of numbers and percentages and presented in tables. Drug interactions were counted and average number of drugs per prescription was calculated.

RESULTS:

Total number of medicines prescribed were 86 types of medicines in 150 prescriptions.

Average medicines prescribed per prescription were 5.6 drugs
Monotherapy was prescribed in 3.3% prescriptions. There were 46.6% prescriptions with less than 5 drugs and 50.1% prescriptions with more than 5 drugs.

Table 1: Drug-Drug Interactions in prescription from Cardiovascular system

S. No.	Drug A	Drug B	Mechanism of Interaction	Desirable (D)/ Undesirable (U)	No of Prescriptions
1.	Digoxin	Torsemide	Hypokalemia induced by diuretics enhances digoxin toxicity i.e. ventricular arrhythmias.	U	2
2.	Digoxin	Furosemide	Hypokalemia induced by diuretics enhances digoxin toxicity i.e. ventricular arrhythmias	U	4
3.	Digoxin	Telmisartan	Telmisartan increases serum levels of digoxin which may lead to digoxin toxicity.	U	3
4.	Digoxin	Amiodarone	Amiodarone will increase the level of digoxin by inhibiting P-glycoprotein . Amiodarone will increase the level or effect of digoxin by basic (cationic) drug competition for renal tubular clearance.	U	3
5.	Digoxin	Ofloxacin	Digoxin and Ofloxacin may compete for renal clearance, increasing ofloxacin levels.	U	1
6.	Telmisartan	Prazosin	Both drugs cause hypotension, this leads to a fall in peripheral vascular resistance and venous return to the heart.	U	4
7.	Furosemide	Telmisartan	Telmisartan increases serum potassium, while furosemide decrease it.	D	5
8.	Metoprolol	Torsemide	Metoprolol increases and Torsemide decreases potassium levels in the blood, Risk of potassium imbalance.	U	1

9.	Diltiazem	Prazosin	Both increase antihypertensive effect. So lower the blood pressure.	U	1
10.	Prazosin	Tamsulosin	Additive vasodilation may lead to postural hypotension.	U	1
11.	Prazosin	Amlodipine	Enhance the blood pressure lowering effect	U	2
12.	Prazosin	Metoprolol	Enhance the blood pressure lowering effect	U	1
13.	Clopidogrel	Rabeprazole	Rabeprazole decreases effects of clopidogrel by altering its metabolism.	U	1
14.	Amiodarone	Hydrochlorothiazide	Amiodarone will increase the level or efficacy of hydrochlorothiazide by basic drug competition for renal tubular clearance	D	1

Table 2: Drug-Drug Interactions in prescriptions from Endocrinology

15.	Metformin	Glimepride	Synergistic decrease in glycemic levels. There is increased risk of hypoglycemia	U	10
16.	Insulin glargine	Liragliptin	Either increases effect of the other by pharmacodynamics synergism	D	2
17.	Insulin Human Regular	Aspirin	Aspirin increases effects of insulin Regular Human so chance of hypoglycemia increase	U	1

Table 3: Drug-Drug Interactions in prescriptions pertaining to corticosteroids.

18.	Prednisolone	Sulfasalazine	Prednisolone decreases level of sulfasalazine by increasing its renal clearance	U	1

Table 4: Drug-Drug Interactions pertaining to Analgesics

19	Ibuprofen	Paracetamol	Ibuprofen act by inhibiting COX1 and COX 2 Paracetamol act on brain's pain and temperature regulating centre	D	1

Table 5: Drug-Drug Interactions in prescriptions pertaining to Central Nervous System

20.	Pregabalin	Escitalopram	Both drugs increase CNS depression	U	1

Table 6: Drug-Drug Interactions pertaining to Antibiotics

21.	Ofloxacin	Azithromycin	Both used together can cause QT prolongation	U	1
22.	Doxycycline	Ceftriaxone	Doxycycline decreases effects of ceftriaxone by opposing its effect on bacterial protein synthesis	U	2

Total number of prescriptions having Drug-Drug Interactions- 49(32.6%)
Total number of desirable Drug-Drug Interactions- 8 (16%) and undesirable ones were - 41 (84%)

DISCUSSION:

Drug-drug interactions are very frequent.

PREVALENCE of DDI:

The present study found prevalence of drug-drug interactions to be 32.6%. Average drug per prescription was found to be 5.6. So this study is in accordance with the study conducted by Marc Oertle in 2012 at Switzerland who analysed total of 1,654,987 prescriptions. On average, 16 different drugs were prescribed for every patient. DDIs were identified in 27% of all prescriptions. Within the most relevant seriousness category, the majority of registered DDI were due to interaction between potassium and potassium-sparing agents, primarily spironolactone, although hyper-kalemia can be lifethreatening.[5]

Kulkarni et al in 2013 conducted a study in South Indian teaching hospital in which 204 prescriptions were analyzed, of which 186 prescriptions i.e 90% prescriptions had 856 DDIs. This is in contrast to what my study identifies a very less 32% prescriptions having DDIs. Kulkarni et al also shows greatest number of DDI from cardiovascular and respiratory disease conditions had the greatest number of drug interactions on average. This is in line with my study also which shows majority of the DDIs relating to Cardiovascular system (30/49 prescriptions) followed by Endocrine system.[6]

Diuretic combinations, diuretic and ACE combinations and digoxin have implicated by Feely et al as the most common DDIs . Similarly, my study has identified Digoxin combinations, Diuretic and ARB combinations (Furosemide and Telmisartan) as one of the most common interacting combinations.[7]

A meta-analysis conducted by Zheng et al in 2017 analysed 4 databases published from 2000 to 2016 and found that 33% of inpatients and 67% of ICU patients had Drug-drug Interactions(DDI) higher than previous years.[8]

POLYPHARMACY:

The present study revealed monotherapy was present in 5(3% prescriptions) while rest 145 (95%) had polypharmacy i.e >1 medicine. This is in line with the study conducted by Akshaya S. Bhagavathula et al in 2021 at Iran showing prevalence of polypharmacy(<10 medicines) was 49% (95% confidence interval: 42–56; $p < 0.01$), hyperpolypharmacy (>10 medicine) was 31% (21–40; $p < 0.01$), among older Indian adults. Polypharmacy was more prevalent in North-east India (65%, 50–79), whereas hyper polypharmacy was prevalent in south India (33%, 17-48).[9]

CONCLUSION:

DDIs are commonly seen in elderly population but also common for any age group having multiple comorbid conditions. The goal should be rational prescribing of multiple medicines. This study assists in understanding the prevalence of DDIs and extent of polypharmacy in North Indian teaching hospital and effective use of drugs in the future.

BIBLIOGRAPGY:

1. Goodman L, Gilman A, Brunton L, Lazo J. and Parker, K. Goodman & Gilman's the pharmacological basis of therapeutics.14 Ed. New York: McGraw-Hill. 2022,24-26.
2. Varghese D, Ishida C, Patel P, Haseer Koya H. Polypharmacy. Treasure Island (FL): StatPearls 2024, 12-16.
3. Ponte ML, Wachs L, Wachs A, Serra HA. Prescribing cascade. A proposed new way to evaluate it. Medicina (B Aires). 2017;77(1):13-16.
4. Prescription Audit. Ministry of Health and family welfare; 2021 [accessed on 2023 Oct 10]. Available from: https://nhsrcindia.org/
5. Oertle M. Frequency and nature of drug-drug interactions in a Swiss primary and secondary acute care hospital. Swiss Med Wkly. 2012 ;142
6. Kulkarni V, Bora SS, Sirisha S, Saji M, Sundaran S. A study on drug-drug interactions through prescription analysis in a South Indian teaching hospital. Ther Adv Drug Saf. 2013;4(4):141-6.
7. Feely J, Barry M. Adverse Drug Interactions. Dublin Clin Med 2005;5:19–22
8. Zheng W.Y, Richardson L.C, Li L,Day R.O.,Westbrook J.I., BayasariM.T. Drug-drug interactions and their harmful effects in hospitalised patients: a systematic review and meta-analysis. Eur J Clin Pharmacol;2018;74,15–27.
9. Bhagavathula AS, Vidyasagar K, Chhabra M, Rashid M, Sharma R, Bandari DK, et al. Prevalence of Polypharmacy, Hyperpolypharmacy and Potentially Inappropriate Medication Use in Older Adults in India: A Systematic Review and Meta-Analysis. Front Pharmacol. 2021 May 19;12:685518.